ENTRANCE EXAMS PROGRAM

FOR THOSE WHO APPLY FOR THE POSTGRADUATE SCHOOL

During the exam you will have to answer questions on your final graduation thesis as well as questions corresponding to the subject of the future research

Questions on the final graduation thesis (master's and specialist's)

1. General provisions.

2. Novelty.

3. Relevance of the applicant's research work.

Mathematical biology. Bioinformatics.

1. Bayesian approach to parameter estimation. Nonparametric tests.

2. String matching algorithms. Finite-state machine, suffix tree and suffix array, regular expressions.

3. Genome annotation. Gene prediction. Functional annotation. Similarity functions. Comparative analysis of genomes.

4. Methods of transcriptome analysis. Tissue-specific transcriptome. Splicing analysis. Applications to disease research and diagnosis.

5. Systems biology. Construction and analysis of regulatory networks. The role of systems biology in the search for targets for drugs.

6. Patterns of inheritance in monohybrid crossing, discovered by Gregor Mendel. Alleles and their interactions.

7. The law of independent inheritance of genes. Features of the inheritance of quantitative traits (polygenic inheritance). Linked inheritance and crossing over.

8. Model organisms used to study the structure and function of genomes. Mapping of genes and genomes. Genome polymorphism.

9. Alignment similarity and homology. Algorithms of dynamic programming. Fast similarity search methods BLAST, FASTA. Statistical significance of alignment. Hidden Markov Models for multiple alignment

Molecular biology.

1. Chemistry as the basis of biology. Water as a medium for biochemical reactions. Electrolytic dissociation, buffer components, polyelectrolytes.

2. Thermodynamics of biological systems. Open and closed systems. Basic thermodynamic functions that can be applied to biological objects. High-energy (macroergic) compounds. Coupling of biochemical reactions with the hydrolysis of macroergs.

3. Amino acids. Peptides. Proteins. Classification, structure, functions. Role in biological systems. Levels of spatial organization of proteins. Protein research methods.

4. Enzymes. Arrangement of enzymes, coenzymes, cofactors. Kinetics of enzymatic catalysis.

5. Nucleotides. Nucleic acids. Nucleic acid research methods.

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7. Transcription. Transcription regulation. Operon regulation.

8. Translation. Genetic code and its properties.

9. Carbohydrates are simple and complex. Structural and reserve polysaccharides. The role of polysaccharides in recognition processes.

10. Glycolysis. Fermentation types of metabolism.

11. The cycle of tricarboxylic acids and its conjugation with anabolism and catabolism.

12. Oxidative phosphorylation. The electron transport chain. Breathing and its types.

13. Lipids. Lipid and carbohydrate metabolism. Synthesis and dissolving of higher fatty acids (beta-oxidation). Synthesis and breakdown of glycogen.

14. Biological membranes. Composition, structure, functions.

15. Transmembrane proteins. Ion channels, receptors. Nerve impulse, its origin and distribution.

16. DNA is the carrier of genetic information. The structure of the DNA double helix. Genes and genomes. Modern methods of deep DNA sequencing.

17. DNA packaging in the nucleus. Histones and histone genes. Non-histone proteins. Nucleosomes. Levels of chromatin organization. Regulatory proteins of chromatin. Structure of active chromatin. Histone code.

23. Genetic code. Features of translation mechanisms in prokaryotes and eukaryotes. Modern ideas about the structure of the ribosome. Mechanisms of regulation of translation. Post-translational modifications of proteins.

24. The life cycle of a cell. Mitotic cycle, mitosis, apoptosis, necrosis. Molecular mechanisms of cell cycle regulation. Cell cycle checkpoints. Tumor suppressor genes. Mechanisms of action of cytostatics.

25. Retroviruses. Genome organization, life cycle and replication features. Retroviral and lentiviral vectors and their use in molecular biology and gene therapy. Modern ideas about the role of retroviruses in evolution.

26. Medical tasks for artificial intelligence application. Artificial intelligence in drug development. Repurposing of drugs. Artificial intelligence in de novo generation of molecules. Reducing heterogeneous data to homogeneous representations for solving problems in medicine, examples.

27. High-throughput screening. Pharmacodynamics. Therapeutic window. PK-PD model. Safety pharmacology study. ADME settings. GLP. Toxicity study. General toxicity. Study of genotoxicity, reproductive toxicity, carcinogenicity.

28. Stages of development of an active pharmaceutical substance. Task setting stage. Stage of laboratory research. Stage scaling. Qualification and validation stage. CAPA and work with deviations. GMP.

29. Laws and principles used in clinical research. Phases of clinical trials. Participants in a clinical study.

30. Innovative, reference drug, generics, generics with improved properties and combined drugs - the difference between the concepts. Bioavailability and therapeutic equivalence. The main stages of the life cycle of drugs. Pharmaceutical development. Excipients for the production of medicinal products.

31. Purposes of patent protection, protected results of intellectual activity. Conditions for the patentability of an invention, intellectual rights for inventions and terms of rights, intellectual rights and rights in rem. Author of RIA, Paris Convention and Patent Cooperation Treaty (PCT).

32. Business management in the field of living systems. Methodology and principles of "lean start-up". Why do startups fail? Types of management paradigms. Turquoise management model. Evolution towards the turquoise management model.

Biophysics.

1. Membrane as a universal component of biological systems. Structural organization of membranes. Lipids. Characterization of membrane proteins. Water as an integral element of biomembranes. Model membrane systems. Monolayer membranes at the interface. bilayer membranes. Proteoliposomes.

2. Membrane potentials. Nernst equation. Donnan equilibrium. Electrodiffusion equation of Nernst-Planck. Ion transport in biological membranes.

3. Fluorescence spectroscopy. The difference between fluorescence and phosphorescence. Relationship between emission spectrum, excitation spectrum and absorption spectrum. Fluorescence quantum yield and excited state lifetime. Fluorescence quenching processes. Fluorescence polarization, its application. Radiative energy transfers and estimation of the distance between chromophore groups in natural compounds. Application of fluorescence to study protein structure.

4. Bionanotechnology. Biological sensors.

5. Nanotechnological methods for the study of biopolymers. Single molecule detection methods.

6. General ideas about genetic engineering, methods for creating recombinant DNA and introducing them into a cell. Application of genetic engineering in basic research in biotechnology.

7. Expression systems for recombinant proteins. Methods for isolation and purification of recombinant proteins.

8. Mass spectrometry. Scope and limits of application of the method of mass spectrometry. Various types of mass spectral instruments and their applications. Methods for ionizing molecules in a mass spectrometer, obtaining a mass spectrum, its interpretation, the concept of a fragmentation scheme. Mass spectrometry in the chemistry of peptides and proteins. The main types of fragmentation of amino acids and peptides. Methods for the study of peptide mixtures.

9. Nuclear magnetic resonance. Nuclear magnetic moment, resonant frequency, shielding and chemical shift. Magnetic relaxation - spin-lattice relaxation and linewidth. NMR spectrometers, sample requirements. Chemical shift and spin-spin interaction, their application in structural studies. Exchange processes. Spectroscopy of the nuclear Overhauser effect. Possibility and limits of application of NMR spectroscopy.

10. Spectroscopy of electron paramagnetic resonance. The physical essence of the phenomenon. The main parameters are g-factor, hyperfine interaction. Spin label method in biology.

11. X-ray diffraction analysis. Requirements for the experiment. Getting and choosing crystals. Diffraction of x-rays on a crystal lattice. Wulf-Bragg conditions. Physical foundations of the method. Fourier transforms. phase problem. Intensity measurements: photographic and diffractometric methods

12. The concept of a mathematical model. Tasks and possibilities of mathematical modeling in biology. The concept of model adequacy to a real object. Principles of constructing mathematical models of biological systems.

13. The structure of the cardiovascular system. Principles of optimality in the organization of branching systems. Classification of vessels. Physical laws of blood flow. Poiseuille's law. Shear rate and stress. Arterial pressure. Central regulation of blood pressure. Baroreceptors in the carotid and cardio-aortic zones. Vascular center. Stress distribution in a loaded vascular wall. Laplace's law.

14. Regulation of blood circulation during changes in the level of activity. Myogenic Bayliss reaction. Distribution of blood flow between various organs at rest and during maximum activity. Metabolic theory of working hyperemia. Defensive reaction. The role of the endothelium in the regulation of organ blood flow. Mechanosensitivity of the endothelium. Endothelial glycocalyx.

15. The structure and function of the heart. Conduction system of the heart. Reverbs. Belousov-Zhabotinsky reaction. Active properties of the heart: contractility, excitability, conduction, refractoriness. Hetero- and homeometric regulation of the pumping function of the heart. Frank-Starling law.

16. Statics and dynamics of the respiratory system. Methods for studying the mechanics of respiration. Airway resistance. Distribution of stresses, deformations, ventilation, blood flow in the lungs. Gas exchange in the lungs. Pulmonary shunts. Respiratory function of the blood. The Bohr effect and its physiological significance.

17. Mathematical modeling of the vascular system. Models with lumped and distributed parameters. Hydraulic impedance of the vasculature. Rheological properties of soft biological tissues. Stress relaxation, creep, hysteresis, anisotropy.

18. Neuron. General information about its structure and functions. Components of a neuron: soma, axon, dendrites, presynaptic ending. Types of neurons. Synaptic transmission. Chemical and electrical synapses.

19. Molecular mechanisms of muscle contraction. The main contractile proteins are actin and myosin. The theory of sliding threads. Calcium regulation of striated muscle contraction, troponin and tropomyosin.

20. Basic models of mathematical biophysics. Lotka-Volterra, Fitz-HughNagumo models, phenomenological model of blood coagulation. Relay mechanisms of signal transmission in distributed excitable biological systems. Kolmogorov-Petrovsky-Piskunov-Fisher and Zeldovich-Frank-Kamenetsky equations.

21. Self-oscillating phenomena in biology and their mathematical models. Necessary conditions for the occurrence of self-oscillations in systems far from equilibrium. Examples of systems with delay. Methods for the qualitative analysis of stationary states, the study of their stability. Dissipative structures in reaction-diffusion systems. A. Turing's instability. The concept of bifurcation. Construction of bifurcation diagrams. Basic concepts of catastrophe theory.

Cell biology.

Cell - General ideas

1.1. What postcellular structures are found in multicellular organisms? How they arise, how they are arranged and what functions do they perform?

1.2. How matrix biosynthesis, combined with random errors and natural selection, lead to the evolution of biological systems. Give examples of matrix biosynthesis. In what cases can the errors that occur during matrix biosynthesis be fixed and transmitted to descendants, and in what cases they can’t?

1.3. What forces are involved in the folding of a protein molecule? Why do many proteins denature in solutions with a high concentration of salts or detergents (surfactants)? What is the Levinthal paradox and how is it resolved?

1.4. Chaperones - what are they? And why are they needed if folding is a spontaneous process?! Why does protein folding with the participation of chaperones (again, a spontaneous process !!!) require ATP?!

1.5. What is the difference between transcription and replication? And what do they have in common? In what processes can RNA be involved in a eukaryotic cell after its transcription is completed? How eukaryotes “manage” to encode multiple proteins on a single gene?

1.6. What methods of light microscopy do you know? How is light microscopy different from electron microscopy? You are studying a microscopic cyclops crustacean. You need to perform the following observations: (A) see how a living crustacean swims in a drop of water (B) study the external structure of the components of the crustacean mouth apparatus (C) look at the location of the muscles inside the crustacean (D) measure the size of mitochondria in the crustacean muscles. What microscopy methods would you use? We assume that the crustacean is transparent and too small to dissect it - you can either look at it as a whole, or make thin slices of it.

1.7. What is the diffraction limit of resolution? What limitations does it create for microscopy? What physical principles are used in ultra-high resolution microscopy to overcome the diffraction barrier?

1.8. What is the physical principle of fluorescence? What fluorescent molecules can be used to visualize intracellular structures? How can they label those intracellular structures? How does a fluorescent microscope, that obtains multi-color pictures, work?

1.9. What does cell culture method consist of? How and why do they grow cells of multicellular animals outside the body? What conditions must be created to maintain their viability?

Plasma membrane: transport, cell contacts

2.1. What surface structures can be present on the cells of bacteria, fungi, plants, animals and protozoa? What is the difference? Why do some cells have a dense cell wall while others do not? How does this relate to water balance?

2.2. What components are present in the plasma membrane? Why is the membrane called “liquid crystal”? What is the peculiarity of the membranes of archaea, bacteria, eukaryotes? How do proteins attach to the plasma membrane?

2.3. What are the functions of membrane proteins? Give examples of membrane proteins that perform different functions. What is the difference between channel proteins, carrier proteins and pump proteins? Give an example of a process in which all three types of transport proteins are involved.

2.4. What compounds are transported across the plasma membrane without the participation of carriers and why? Why can water, although polar, pass through the membrane without the participation of carriers? Why are these water carriers still present in some cells? Why does sodium transport the membrane only by facilitated diffusion, but the I_3^- ion can cross the membrane by simple diffusion?!

2.5. The ratio of primary-active and secondary-active transport through the membrane. What proteins are responsible for creating a difference in ion concentrations on both sides of the plasma membrane of: an animal cell? plant cell? aerobic bacteria cells? fermenter bacteria cells?

2.6. Calcium. What transport systems are involved in the transportation of calcium across cell membranes. In what intracellular processes is calcium involved? Give examples of these processes.

2.7. Membrane potential. How is it formed? How to calculate equilibrium potentials for ions on a membrane? How to calculate the membrane potential, knowing the equilibrium concentrations of ions? What ions are most important for the formation of the membrane potential of an ordinary animal cell? The role of which increases with the action potential of the neuron? Cardiomyocyte?

2.8. The action potential of the nerve cell and cardiomyocyte. What phases does the action potential consist of and what mechanisms provide it? How is an action potential different from a resting potential? How the electrical properties of the membrane provide the pacemaker activity of the heart?

2.9. What cell contacts are present in an epithelial cell? Describe them. How do they differ from migrating fibroblast contacts? Which of these contacts are calcium dependent and which are not?

2.10. Synapse. Describe the structure of a synapse. What are the structural and functional differences between electrical and chemical synapses? What is the difference between the synapse of the central nervous system and the neuromuscular synapse? Describe the main processes that occur during the transmission of excitation from presynapse to postsynapse.

Cytoskeleton

3.1. Microtubules: structure and location inside the cell. Structures formed by microtubules. Which motor proteins are associated with microtubules and how they function.

3.2. What is microtubule dynamics based on? In what processes in the cell can it manifest itself? What poisons affect the dynamics of microtubules in the cell?

3.3. Microfilaments: structure and location inside the cell. Structures formed by microfilaments. What proteins, binding to microfilaments, determine their stability and bonding with each other and other intracellular components?

3.4. Ameboid movement vs flagella: differences and mechanisms. What is the difference between different variants of amoeboid movement?

3.5. Myosins: variety and mechanism of work. How do processive myosins differ from non-processive ones? Myosin V as an example of processive myosin.

3.6. Muscle contraction. The structure of myosin II. How can non-processive myosin be involved in muscle contraction? What proteins are involved in the regulation of contraction of smooth muscle and striated muscle. How does rigor mortis occur?

Bioenergy

4.1. Respiratory chain of mitochondria in animals. Comparative characteristics of the respiratory chain of animal mitochondria and the respiratory chain of plant mitochondria.

4.2. Comparative characteristics of the respiratory chain of animal mitochondria and the respiratory chain of aerobic bacteria.

4.3. Aerobic and anaerobic respiration. Differences between respiration and fermentation.

4.4. Photosynthetic ETC - non-cyclic electron transfer.

4.5. Photosynthetic ETC - cyclic electron transfer.

4.6. Comparative characteristics of photosynthetic and respiratory ETC.

Nucleus and cytoplasm

5.1. Nuclear-like structures of prokaryotes. Main core components.

5.2. Nuclear porous complex: structure and components. Nuclear import and export systems.

5.3. Nuclear lamina: components and functions. The fate of the nuclear lamina in the cell cycle.

5.4. Nucleolus: structure and components. Nucleolar organizer. Ribosome assembly.

5.5. Histones and nucleosome. Histone modifications. Levels of chromatin compaction. Structural and functional differences between euchromatin and heterochromatin.

5.6. Endoplasmic reticulum. Structural and functional differentiation of granular and agranular EPR. Biosynthesis of membrane and secreted proteins. Differences for single-pass and multi-pass proteins.

5.7. Golgi apparatus. Sorting of proteins and membranes in a eukaryotic cell. Lysosomes - structure and functions. Phagocytosis. Synaptic vesicles: their similarities and differences with lysosomes.

5.8. Endosymbiotic organelles: origin and features. Primary and secondary endosymbiosis. Organization of the genetic apparatus. Replication and transcription in human mitochondria. Mitochondrial Eve. Haplogroups. Cytoplasmic inheritance.

5.9. Mitosis and meiosis: comparative characteristics. The fate of chromosomes during mitosis and meiosis. The fate of the cytoskeleton during mitosis and meiosis.

5.10. The position of meiosis in the life cycle of different organisms. The emergence and role of the sexual process in eukaryotes. Comparative characteristics of spermatogenesis and oogenesis in mammals.

Fundamentals of Histology

6.1. Tissue. Variety of epithelial tissues. Distribution of different types of epithelium in the human body. Types of secretion in the glands.

6.2. Variety of connective tissues. The structure and distribution of skeletal tissues in the human body.

6.3. Biogenesis and functions of blood cells.

6.4. Muscle tissue: differences in the organization of the contractile apparatus and the regulation of contraction in different types of muscles. Muscle tissue: structure and localization in the body.

6.5. Glial cells: diversity and function. Blood-brain barrier.

6.6. Cancer transformation of cells: main genetic markers. Cancer cell transformation: approaches to therapy.